

Notice of Allowability	Application No.	Applicant(s)	
	10/828,278	JOHNSON, MICHAEL R.	
	Examiner	Art Unit	
	Zachary C. Tucker	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 8 November 2006.
2. ☒ The allowed claim(s) is/are 82-121, 124-127, 129-152 and 157-169.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|---|---|
| <ol style="list-style-type: none"> 1. <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3. <input checked="" type="checkbox"/> Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date <u>21Apr04, 14Mar06</u> 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | <ol style="list-style-type: none"> 5. <input type="checkbox"/> Notice of Informal Patent Application 6. <input type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date _____. 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance 9. <input type="checkbox"/> Other _____. |
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EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorizations for this examiner's amendment were given in two telephone conversations with James J. Kelly on 14 and 15 November 2006.

IN THE CLAIMS -

Claims 87, 122, 123, 128 and 153-156 are cancelled.

In claim 82, page 3 of the listing of claims provided with the Preliminary Amendment filed 22 November 2004 (11/22/2004), in the 4th line of the claim, **delete** the following:

–restoring mucosal defense, preventing ventilator-induced pneumonia,–

and in its place, insert the following:

treating ventilator-induced pneumonia

also in claim 82, page 7 of the same Preliminary Amendment, in the 5th and 6th lines down from the top of the page, **delete** the following:

–or a nitrogen atom, wherein at most three Q in a ring are nitrogen atoms –

Art Unit: 1624

In claim 88, page 8 of the listing of claims provided with the Preliminary Amendment filed 22 November 2004 (11/22/2004), in the 1st line of the claim, **delete** the word:

~~—preventing—~~

and in its place, insert the following:

treatment of

In claim 125, at page 12 of the listing of claims included with the Preliminary Amendment filed 22 November 2004 (11/22/2004), in the 6th and 7th lines of the claim, **delete** the following (do not delete the period at the end of the claim):

~~—; and at most 2 Q in a ring are nitrogen atoms—~~

In claim 127, at page 12 of the listing of claims included with the Preliminary Amendment filed 22 November 2004 (11/22/2004), in the 4th and 5th lines of the claim, delete the following (do not delete the period at the end of the claim):

~~—; and at most 1 Q in a ring are is a nitrogen atom”~~

end of amendments

***Requirement for Restriction
~and~
Election of Species***

A written Requirement for Restriction was mailed to applicant 13 October 2006. In reply to the Requirement, filed 8 November 2006, applicant indicated election of the invention of Group I, the methods wherein in the compound of formula (I) as specified in claim 82, the variable "Q"-containing ring is a phenyl ring, all "Q" are carbon atoms, that is.

Because no prior art anticipating or otherwise rendering the claimed invention unpatentable was found in the search conducted by the examiner, non-elected subject matter has been removed from the claims by the attached Examiner's Amendment, authorized by applicant's counsel.

Allowable Subject Matter

Claims 82-121, 124-127, 129-152 and 157-169 are allowed.

The following is an examiner's statement of reasons for allowance:

The compound of formula (I), which is administered as the therapeutic agent in the method according to instant claim 82, which is the independent claim in the application, is of the same scope of the compounds *per se*, allowed in the patent that issued from the parent application to the instant application (SN 10/076,551, now US 6,858,614). The instant application was filed for the reason that in the prosecution of the parent application, the examiner required restriction between compounds of different chemical structure (based on the "Q"-containing ring), different *therapeutic* methods wherein those different compounds are employed as the therapeutic agent, and various methods of blocking sodium channels, with the various compounds of differing chemical structure.

Art Unit: 1624

The compounds per se were elected by applicant, and ultimately allowed, at which time the examiner rejoined the nonelected claim drawn to blocking sodium channels therewith.

Because the claim in the parent application that was drawn to blocking sodium channels with formula (I) compounds did not recite any *therapeutic* limitations, it was deemed by the examiner not to be overlapping with the claims in that application which were drawn to methods of treating various diseases and conditions with the formula (I) compounds. Thus, the claim of the patent drawn to a method of blocking sodium channels, cannot be used as a reference in a double patenting rejection against the instant claims; a double patenting rejection of the instant claims in view of the method claim in US 6,858,614 is not permitted.

Compounds according to formula (I) are neither disclosed nor suggested in the prior art. They are based on a pyrazinoylguanidine core structural motif, the prototypical example of which is the diuretic drug amiloride, which has been known for a long time (US 3,313,813 to Cragoe, Jr.). References cited in the Information Disclosure Statements (IDS) of 21 April 2004 and 14 March 2006 represent the closest prior art with respect to the subject matter of the allowed claims. Particularly of note is R. F. Epand et al, *British Journal of Cancer*, vol. 63(2), pages 247-251 (1991). This article is cited on page 5 of the PTO-1449 form that accompanied the former IDS.

Epand et al teaches a group of pyrazine-based inhibitors of Na⁺/H⁺ transport, based on the amiloride pharmacophore. On page 248, in the table, the second structure depicted is similar to a compound which would be employed in the method according to claim 82. The "Q" containing ring in formula (A) is a phenyl ring, and the hydroxy group is bonded at the 4-position. This compound would be embraced by formula (I) of the instant

Art Unit: 1624

claims, except this compound is excluded from the scope of formula (I) because of the proviso which limits the sum of "o" and "p" to a number from 4 to 10, when "x" is a single bond, in the linker moiety connecting the "Q" variable containing ring structure to the pyrazinoylguanidine core. The Epand et al compound in question only has two methylene units between the guanidinyll group and the phenolic group, not enough to meet the limitations of formula (I). Epand et al does not suggest any structural modifications to this sole phenolic compound, it is the only one of its type reported in the article.

One of the allowed claims is drawn to the method according to instant claim 82, wherein the formula (I) compound is administered as a composition which also comprises a P2Y2 agonist. At the time the invention was made, one of ordinary skill understood the scope of this claim, because as a class, P2Y2 agonists were recognized as therapeutic agents to increase mucociliary clearance. The following reference:

Kellerman, D. "P2Y2 Receptor Agonists. A New Class of Medication Targeted at Improved Mucociliary Clearance" Chest, vol. 121(5), supplement, pages 201S-205S.

Is evidence to this effect.

Insofar as applicant's other issued U.S. patents disclosing and claiming sodium channel blocker compounds based on the same core amiloride motif, none of those patents poses any double patenting issues with respect to the instant claims, although the language of the method claims in these issued patents is the same, or substantially the same, because the compounds with which the methods are practiced are different. There is no overlap between any of the instantly claimed subject matter and subject matter claimed in applicant's other patents in the present series.

These issued patents thus far are:

Art Unit: 1624

US 6,858,614, US 6,828,615, US 6,903,105, US 6,995,160, US 7,026,325, US 7,030,117 and US 7,064,129.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

All Post-Allowance Correspondence concerning this application must be mailed to:

Mail Stop Issue Fee
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Or you can fax them to the Office of Patent Publications at 703-872-9306, in order to expedite the handling of such correspondence as amendments under 37 CFR 1.312; information disclosure statements, and formal drawings. Sending Post-Allowance papers to Technology Center 1600 will only cause delays in matching papers with the case.

For information concerning status of correspondence sent after receipt of the Notice of Allowance, please contact the Correspondence Branch at (703) 305-8027. The Notice of Allowance also has an insert containing contact information on other items, including Issue Fees, receipt of formal drawings and the status of the application.



Zachary C. Tucker
Primary Examiner
Art Unit 1624